at page 15, lines 7-9. New claims 34 and 38-40 are supported by the specification, for example, at page 5, lines 28-30, page 16, lines 26-31 and page 18, line 29 to page 19, line 28. No new matter is introduced by the amendment of claim 1 or by the new claims.

Claim 28 has been allowed, and claim 14 has been found free of the cited art. Claims 1, 3-5, 8-13 and 15-17 stand rejected. Applicants respectfully request reconsideration of the rejections based on the following remarks.

Rejections Over Cahalan et al. and Goldstein

The Examiner rejected claims 1, 3, 4, 8-12 and 15 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,308,641 to Cahalan et al. (the Cahalan patent) in view of U.S. Patent 5,613,982 to Goldstein (the Goldstein patent). The Examiner maintained the rejection over this combination of references in view of Applicants' arguments that there was no motivation to combine the references. While Applicants do not agree with the Examiner's assertions, Applicants have amended claim 1 to more particularly point out their claimed invention in view of advancing prosecution of the case. Applicants respectfully request reconsideration of the rejection based on the following comments.

The Cahalan patent is directed to an approach for attachment of proteins to solid substrates having a range of compositions, including tissue. However, the Cahalan patent discloses use of a spacer compound for attachment of the compounds to the substrate. While the Cahalan patent teaches use of a crosslinking agent for performing the attachment process (see, for example, column 4, lines 58-60), the Cahalan patent stresses that the spacer compound intervenes between the substrate and the biologically active compound. See column 4, lines 62-66. The Cahalan patent teaches away from Applicants' claimed invention involving the direct crosslinking of a growth factor to a substrate.

The Goldstein patent explicitly teaches away from the use of aldehyde crosslinking agents. At column 1, line 66 to column 2, line 13, the Goldstein patent describes crosslinked tissue as being non-viable due to cytotoxicity of glutaraldehyde crosslinked tissue. Specifically, the Goldstein patent stresses cell repopulation of tissue (see column 9, line 33 to column 12, line 34. Since aldehyde crosslinking agents can be detrimental to cellular repopulation, the Goldstein patent teaches away from aldehyde crosslinking of tissue. Since claim 1 indicates the presence of aldehyde crosslinking agents, the Goldstein patent clearly teaches away from the claimed invention.

Since the Cahalan patent teaches away from the direct crosslinking of a biologically active compound with a substrate and since the Goldstein patent teaches away from aldehyde crosslinking agents, the combined disclosures of the Cahalan patent and the Goldstein patent do not lead to Applicants' claimed invention. Therefore, the combined disclosures of the Cahalan patent and the Goldstein patent do not render the claimed invention obvious. Applicants respectfully request withdrawal of the rejection of claims 1, 3, 4, 8-12 and 15 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent in view of the Goldstein patent.

Rejections Over Cahalan et al., Goldstein and Bayne et al.

The Examiner appears to have rejected claims 13, 16 and 17 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent and the Goldstein patent as applied to claims 1, 3, 4, 8-12 and 15, and further in view of EP application 0476983 to Bayne et al. (the Bayne EP application). The Examiner cited the Bayne EP application for disclosing VEGF and the culturing of endothelial cells. Applicants note that the Examiner did not comment on the disclosure of elements of claim 17 in the cited references. Applicants respectfully request clarification of the rejection of claim 17. In general, Applicants believe that the Bayne EP application does not make up for the deficiencies of the remaining references. Applicants respectfully request reconsideration of the rejection based on the following comments.

As noted above, the Cahalan patent and the Goldstein patent teach away from Applicants' claims directed to the direct bonding of a biological agent with a substrate using aldehyde crosslinking agents. The Bayne EP application does not teach or suggest the bonding of a growth factor with a substrate. Therefore, the Bayne EP application does not make up for the deficiencies of the Cahalan patent and the Goldstein patent. Since the Cahalan patent and the Goldstein patent teach away from Applicants' claimed invention and the Bayne EP application does not teach or suggest Applicants' claimed bonding approach, the combined disclosures of the Cahalan patent, the Goldstein patent and the Bayne EP application do not render Applicants' claimed invention obvious. Applicants respectfully request withdrawal of the rejection of claims 13, 16 and 17 under 35 U.S.C. §103(a) as being unpatentable over the Cahalan patent and the Goldstein patent as applied to claims 1, 3, 4, 8-12 and 15, and further in view of the Bayne EP application.

In response to the Examiner's request for information on copending applications that set forth similar subject matter to the present claims, Applicants note that the parent application (09/014,087) is copending. Applicants believe that this application is being examined by the same Examiner as the present case. Therefore, Applicants do not believe that it is necessary to provide a copy of the copending application. Applicants also note copending application 09/459,451 entitled "Medical Articles Prepared For Cell Adhesion," although Applicants do not believe that this application is relevant to the current prosecution.

CONCLUSIONS

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

Application No. 09/186,810

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

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April 25, 2002
Date

Molly A. McClellan
Molly A. McClellan

Application No. 09/186,810

ATTACHMENT
MARKED-UP AMENDMENT

Claim 1 has been amended as follows:

1. (Six Times Amended) A prosthesis comprising a substrate and a polypeptide growth factor associated with the substrate by covalent bonding using crosslinking agents, antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, wherein the crosslinking agents comprise at least two aldehyde functional groups that form covalent bonds to link the crosslinking agent directly with the polypeptide growth factor and the substrate, the polypeptide growth factor associated with the substrate being effective to stimulate association of viable cells with the substrate, and the substrate [being selected from the group consisting of heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, submucosa and bioresorbable polymers].

New claims 29-40 have been added as follows:

--29. (New) The prosthesis of claim 28 wherein the biocompatible substrate comprises tissue.

30. (New) The prosthesis of claim 28 wherein the biocompatible substrate comprises a synthetic material.

31. (New) The prosthesis of claim 28 wherein the substrate comprises a bioresorbable material.

32. (New) The prosthesis of claim 28 wherein the polypeptide growth factor is bonded to the substrate with a crosslinking agent.

33. (New) The prosthesis of claim 28 further comprising an adhesive, the adhesive being associated with the polypeptide growth factor and the substrate.

34. (New) A prosthesis comprising a substrate and a polypeptide growth factor associated with the substrate by antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, the polypeptide growth factor associated with the substrate being effective to stimulate association of viable cells with the substrate.

35. (New) The prosthesis of claim 34 wherein the biocompatible substrate comprises tissue.

36. (New) The prosthesis of claim 34 wherein the biocompatible substrate comprises a synthetic material.

37. (New) The prosthesis of claim 34 wherein the substrate comprises a bioresorbable material.

38. (New) The prosthesis of claim 34 wherein the polypeptide growth factor is associated with the substrate by antibody-antigen associations.

39. (New) The prosthesis of claim 34 wherein the polypeptide growth factor is associated with the substrate by specific binding protein-receptor associations.

40. (New) The prosthesis of claim 34 wherein the polypeptide growth factor is associated with the substrate by enzyme-substrate associations.–